Testimony
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Subcommittee on National Security, Emerging Threats, and International Relations
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The Role of HHS in the Development and Acquisition of Medical Countermeasures for Chemical, Biological, Radiological and Nuclear (CBRN) Threats

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Good afternoon, Mr. Chairman, Mr. Kucinich and Subcommittee members. I am Stewart Simonson, Assistant Secretary for Public Health Emergency Preparedness, Department of Health and Human Services (HHS). I appreciate the opportunity to share with you information on the Department's progress in research, development and acquisition programs for medical countermeasures, particularly with regard to the implementation of the Project BioShield Act of 2004 ("Project BioShield"). These programs are vital components of our strategy to protect the Nation from threats posed from chemical, biological, radiological and nuclear (CBRN) threats. Defending against such threats is a top priority for the Bush Administration and having an appropriate armamentarium of medical countermeasures is a critical element of the response and recovery component of the President's "21st Century Strategy for Biodefense." The acquisition and ready availability of medical countermeasures, such as antibiotics, antivirals, monoclonal and polyclonal antibodies against infectious threats, therapies for chemical and radiation-induced illnesses, and vaccines to protect against exposure from biological agents are essential to our Nation's preparedness and response capabilities.

Protecting Americans

The events of September and October 2001 made it very clear that terrorism- indeed bioterrorism- is a serious threat to our Nation and the world. The Bush Administration and Congress responded forcefully to this threat by providing funding to strengthen our medical and public health capacities to protect our

citizens from future attacks. Specifically, substantial increases in funding for research, development and acquisition of medical countermeasures against biological threats were directed to the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention's Strategic National Stockpile (SNS or "the Stockpile"). To further encourage the development of new medical countermeasures against chemical, biological, radiological and nuclear agents and to speed their delivery and use should there be an attack, President Bush, in his 2003 State of the Union address proposed and Congress subsequently enacted Project BioShield. The Special Reserve Fund, appropriated with $5.6 billion was created to assure developers of medical countermeasures that funds would be available to purchase these critical products for use to protect our citizens.

HHS Research Efforts to Respond to CBRN Threats

Dr. Anthony Fauci, the Director of the National Institute of Allergy and Infectious Diseases (NIAID), a component of the NIH, will be testifying here today regarding the role of his institute in research and development of needed medical countermeasures for CBRN threats. NIAID is leading the Federal research enterprise in this area and Dr. Fauci will detail the Institute's efforts. I will focus my testimony on the efforts at HHS to lead the acquisition of medical countermeasures for the SNS.

The Strategic National Stockpile Today

The wake-up call that we received in the fall of 2001 highlighted the gaps in our medical countermeasure armamentarium and we immediately sought to address them. Although much remains to be done, we have made significant progress in building our Strategic National Stockpile from that time to what we have on-hand today. For example, our smallpox vaccine stockpile has grown from 90,000 ready-to-use doses in 2001 to enough vaccine to protect every man, woman, and child in America. Major strides have been made in building our medical countermeasure reserve against anthrax, plague, and tularemia. We are now able to protect and treat millions of Americans in the event of an attack with one of these agents. We have taken the botulinum antitoxin program started by the Department of Defense in the early 1990s to completion and we are now building our botulinum antitoxin stockpile further. We have also built our stockpile of countermeasures to address the effects of radiation exposure with products such as Prussian Blue and diethylenetriaminepentaacetate (DTPA). These countermeasures act to block uptake or remove radioactive elements such as cesium, thallium, or americium from the body after they are ingested or inhaled. Potassium iodide, a drug that can protect the thyroid from the harmful effects of radioactive iodine, is also in the Stockpile.

The Strategic Approach to Addressing Medical Countermeasure Gaps

The initial focus of our efforts to protect the Nation was aimed largely at those threats that could do the greatest harm to the greatest number of our citizens. Among biological threat agents, smallpox and anthrax are widely recognized as

having the greatest potential to cause catastrophic harm. A sense of urgency has pervaded our efforts and we have defined new ways of doing business. Our new national security environment demands accelerated product development timelines and new paradigms of interactions between industry and government with increased risk-sharing and enhanced intra-governmental collaboration.

The focal point for USG interagency efforts to prioritize and coordinate medical countermeasures acquisition programs is the Weapons of Mass Destruction Medical Countermeasures (WMDMC) Subcommittee ("WMDMC Subcommittee"). HHS, along with representatives from the Department of Homeland Security (DHS) and the Department of Defense (DoD), co-chairs the WMDMC Subcommittee and stakeholders from throughout the USG are represented on it. Because HHS is the primary federal agency responsible for the development and acquisition of priority medical countermeasures, we have a major leadership role in the WMDMC Subcommittee.

The cornerstone of any sound acquisition program is the determination and prioritization of requirements and this is a primary activity of the WMDMC Subcommittee. In setting priorities for medical countermeasure acquisition under Project BioShield, the WMDMC Subcommittee considers a number of factors. The credibility and immediacy of the specific threats are driving factors and are informed by Material Threat Assessments (MTAs) conducted by the DHS. Dr. John Vitko, here today representing DHS, will provide insight into these efforts.

Other factors include an evaluation of the availability of appropriate countermeasures, both current and projected, and the target population for which the medical countermeasure would be used. In addition, logistical issues are considered such as the feasibility of deployment in a public health emergency, shelf life, and the storage and maintenance requirements. Project BioShield also requires a number of findings by the Secretaries of Homeland Security and HHS prior to an acquisition commencing. These findings include:

- Determination of material threat against the US population sufficient to affect national security. This determination is made by the Secretary of Homeland Security.
- Determination that countermeasures are necessary to protect public health. This determination is made by the Secretary of HHS.
- Determination of the appropriateness of funding acquisition of the countermeasure with the Special Reserve Fund (SRF). This determination is made by the Secretary of HHS.

Once these determinations are made, a joint recommendation for the acquisition is presented to the White House by the two Secretaries. If approved, Congress is notified and HHS executes the acquisition program.

The process that I have outlined for you has been successfully implemented three times since the enactment of Project BioShield less than one year ago. HHS has completed contract awards for acquisitions of the next-generation recombinant protective antigen (rPA) anthrax vaccine, the current-generation

licensed anthrax vaccine (Anthrax Vaccine Adsorbed, AVA), and the pediatric formulation of potassium iodide. Additionally, the acquisition process is in the final execution phases for several other needed medical countermeasures including anthrax therapeutics, botulinum antitoxin, and a next-generation smallpox vaccine.

This robust interagency process mines the expertise of subject matter experts in the scientific and intelligence communities to define requirements for medical countermeasures and enable policy makers to identify and evaluate acquisition options to address immediate and future needs.

Application of the Strategic Approach: Anthrax.

The efficiency and effectiveness of the steps used to identify, prioritize, and acquire needed medical countermeasures is best exemplified by our efforts to protect the Nation in the event of an anthrax attack. It will also illustrate intra-agency and interagency processes.

Although anthrax is not transmissible from person-to-person, an attack involving the aerosol dissemination of anthrax spores, particularly in an urban setting, is considered by public health experts to have the potential to cause catastrophic damage. The potential for large-scale population exposure following aerosol release of anthrax spores, the threat demonstrated by the anthrax letters, and our knowledge that anthrax had been weaponized by state-actors, highlighted

the nature of the threat. The Secretary of Homeland Security determined that anthrax posed a material threat to the Nation. Because untreated inhalation anthrax is usually fatal, the Secretary of HHS identified anthrax as a significant threat to public health.

The approach to protect citizens against this threat demanded immediate, intermediate and long-term strategies and requirements. First, the existing stockpile of antibiotics in the Strategic National Stockpile was increased. Second, there is a need for a licensed vaccine to be used not only for pre-exposure protection for laboratory and other workers at known risk for anthrax, but for use along with antibiotics after an exposure which could decrease the currently recommended 60-day course of antibiotic therapy. Anthrax spores are stable in the environment and would have a profound impact if released in an urban population. Therefore, availability of a vaccine may be a critical requirement for repopulation and restoration of the functionality of any exposed area.

Due to limitations inherent in the currently available anthrax vaccine, there is consensus in the scientific community about the need to develop and acquire a next-generation anthrax vaccine using 21st century technologies An assessment of developing technologies was undertaken by HHS experts in the fall of 2001 and the decision was made that there was a sufficient scientific foundation, including a detailed understanding of the pathogenesis of anthrax and how

anthrax vaccines provide protective immunity, to support the aggressive development of a next generation vaccine consisting of recombinant protective antigen (rPA). The research undertaken to develop this vaccine, spanning more than a decade, was conducted in large part by the United States Army Medical Research Institute of Infectious Diseases at Fort Detrick, Maryland.

HHS defined a three-stage development and acquisition strategy with open competition for awards at each stage. The early and advanced development programs were supported by the NIAID with contract awards in September 2002 and 2003, respectively. These were milestone-driven contracts with well-defined deliverables including the manufacture of clinical-grade vaccine, the conduct of Phase I and Phase II clinical trials, and consistency lot manufacturing of vaccine. Large-scale manufacturing capacity would be required to support the civilian requirement for this medical countermeasure, which was defined by the WMD Subcommittee to be the initial protection of up to 25 million persons. Senior officials from several Departments of the USG evaluated acquisition options to achieve this requirement and, in the fall of 2003, approved the decision to pursue this acquisition of rPA anthrax vaccine.

An evaluation of the NIAID rPA anthrax vaccine development program indicated that it was robust enough to suggest that the rPA vaccine could become a licensed product within 8 years. In March 2004, the acquisition program for this vaccine, under the direction of my office, was launched using the Special

Reserve Fund created in the FY 2004 DHS appropriations bill. Utilizing a robust technical and business evaluation process, we reviewed multiple proposals and negotiated a contract for the acquisition of 75 million doses of the vaccine (anticipating a three-dose regimen). Using a milestone and deliverables approach similar to the ACAM2000 smallpox vaccine development and acquisition program, and the rPA anthrax vaccine development contracts at NIAID, the rPA vaccine BioShield acquisition contract lays out an ambitious program for the production of this vaccine. In accordance with Project BioShield, a critical aspect of this acquisition contract is the fact that no payment for product is made until a usable product is delivered to the SNS. While awaiting delivery of the rPA anthrax vaccine to the SNS, my office awarded a contract last month for 5 million doses of the currently licensed AVA vaccine to support immediate requirements. Delivery of this product to the Stockpile began soon after contract award and over one million doses of the licensed anthrax vaccine are now in the SNS.

Application of the Strategic Approach: Other Medical Countermeasures

In an effort to fill other medical countermeasure gaps, we have made progress in contracting for products that are or will soon be delivered to the SNS.

Potassium Iodide.

In March 2005 a contract was awarded under Project BioShield for a pediatric liquid formulation of potassium iodide, a drug that helps limit risk of damage to the thyroid, from radioactive iodine. This formulation is aimed at young children

who have difficulty taking pills and are at the highest risk of harmful effects from exposure to radioactive iodine. This acquisition will provide needed protection for at least 1.7 million children. Product delivery began last month and should be completed by the end of the fiscal year.

Ongoing Project BioShield activities.

In addition to the acquisition contracts that have been awarded since enactment of Project BioShield, there are several other important BioShield procurement-related activities underway. We are engaged in contract negotiations for anthrax therapies, and we are continuing to move forward on the acquisition of an antitoxin treatment for botulism. Furthermore, HHS has moved forward with the initial stages of an acquisition program for a next generation smallpox vaccine to meet a requirement for this product that addresses the millions of U.S. citizens who have contraindications for existing smallpox vaccines. A draft RFP was released last month; the final RFP will be released following review of industry comments. We also anticipate releasing a draft RFP for industry comment next month to address requirements for therapeutics for acute radiation syndrome.

Finally, in anticipation of yet to be determined requirements, we actively monitor the state of the medical countermeasure pipeline-- both within and outside the government--- by evaluating USG research and development portfolios and engaging industry through the publication of Requests for Information (RFIs). For example, we have recently released three RFIs to assess the timeline to

maturity of medical countermeasures to treat nerve agent exposure, acute radiation syndrome, and additional products that might be available to treat anthrax. These requests are a key tool for HHS to dialogue with industry partners and to inform the development of sound USG acquisition strategies.

Priority Setting Beyond Smallpox and Anthrax

The approach taken to rapidly expand our Nation's response capacity to meet the medical and public health impact of either a smallpox or anthrax attack demonstrate our national resolve to address these threats. However, in many ways, anthrax and smallpox represent the "low hanging fruit" for medical countermeasure research, development and acquisition and was largely made possible by a substantial research base developed by USAMRIID and NIH. There was consensus that these were our highest priorities and we had countermeasures available or relatively far along in the development pipeline to permit acquisition. Given an almost endless list of potential threats with finite resources to address them, prioritization is essential to focus our efforts. We rely heavily upon our interagency partner, the Department of Homeland Security, to provide us with a prioritized list of threats along with material threat assessments that will include reasonable estimates of population exposure. This information is critical for future strategic decision making regarding how best to focus our National efforts in countermeasure development and acquisition, including whether in the short-term, the so-called "one-bug, one-drug" approach should

continue while simultaneously investing in more broad-spectrum prevention and treatment approaches for the longer term.

Novel and Emerging Threats

The initial efforts for medical countermeasure development and acquisition have been rightfully focused on those threat agents known to have the potential to inflict catastrophic harm on our Nation. In addition, HHS and NIH are investing in efforts to address threat agents that we might face in the future, including engineered threats.

As is also the case for the known threat agents, we are dependent upon our colleagues at DHS to identify and prioritize these threats. One of the most recognized potential engineered threats is antibiotic-resistant anthrax, and the HHS, NIH and the U.S. Food and Drug Administration (FDA) accomplishments to date in facilitating the development and acquisition of anthrax vaccines and therapeutic antitoxins have made an important impact on reducing our vulnerabilities in this area. In addition, NIH has made a robust investment in the development of novel antimicrobial agents and in addressing all aspects of antibiotic resistance. For example, investments have been made in the development of antibacterial agents that could potentially be useful against a broad spectrum of species and a wide range of drug resistance mechanisms. Finally, NIH is working with DoD to leverage medical countermeasure programs and resources of mutual interest.

Challenges to Rapidly Expanding the Strategic National Stockpile

Although defining priorities and quantifying the size of the threat to the population are the key steps to focus our efforts, we must be mindful of the realities of the spectrum of efforts needed along the research and development pipeline to produce a useable medical countermeasure. The process of defining required specifications for a countermeasure often reveals few, if any, candidates in the pipeline. Basic research and early development efforts, even when robustly funded, often take years before a concept is mature enough for advanced development. The development of medical products —whether for cancer, influenza, or anthrax – is a complex, lengthy, and expensive process. Ultimate licensure, approval or clearance from FDA requires the rigorous accumulation of sufficient data in humans and animals to establish the safety and efficacy of the product for a specific use and the ability to consistently manufacture the product to meet the appropriate standards. It is important to note that a unique aspect of the pathway for medical countermeasures is the need to establish efficacy either using surrogate markers (such as the human immune response) or, using appropriate animal models, under the "Animal Rule" (*Federal Register* 67:37988-37998, 2002) because demonstration of efficacy against the actual diseases in humans is most often not feasible either because the disease does not occur naturally or for the obvious ethical reasons that prevent exposing humans to the threat agent. The USG is working to provide support for the developers of priority medical countermeasures through the research and development phases,

and, when a product has reached the advanced development stage Project BioShield provides an important incentive for manufacturers to take the product the rest of the way through the pipeline. And, as I have outlined here today, in the less than eleven months since Project BioShield was enacted, the incentive has expedited final development of several products for the Stockpile.

Conclusion

In closing, I must emphasize that the number of threat agents against which we could guard ourselves is endless and new and emerging threats introduced by nature or man will present continuing challenges. Although we cannot be prepared for every threat, we have the ability to create a strategic approach to identifying and combating the greatest threats. HHS and its agencies including NIH, CDC, and FDA, have a clear mandate from President Bush and Congress to lead the charge in this arena. We have already made important strides and will continue to work to address the obstacles identified. Mr. Chairman, I look forward to working with you and members of the Subcommittee to address the challenges of bioterrorism preparedness and its impact on public health.

I will be happy to answer any questions you may have.